

Summary of Hypotheses Identified Through The Lewin Group's Targeted Literature Review

The Lewin Group identified 29 hypotheses for potential inclusion in the National Children's Study. These hypotheses were identified from a review of relevant scientific literature focusing on eight targeted research areas:¹

- Asthma and respiratory illnesses
- Childhood cancers
- Endocrine disruptors
- Environmental toxicants
- Injury
- Neurodevelopment and Biobehavioral Development
- Other specialized research areas, which includes Obesity and Sudden Infant Death Syndrome.

This document presents a series of 29 hypotheses identified in the targeted literature review of 49 articles, and a supplemental review of an additional 23 articles that specifically focused on the targeted research areas.

¹ The *Background on Targeted Research Areas* section of this document describes the research approach and methodology that led The Lewin Group to categorize the reviewed literature into the above-mentioned targeted research areas.

Targeted Research Area: Asthma and Respiratory Illnesses

Hypothesis #1: Infections in early childhood have a protective effect against asthma.

Hypothesis #2: Endotoxin exposure in childhood may have a protective effect against the development of asthma.

Hypothesis #3: Maternal exposures to environmental agents (e.g., indoor allergens or environmental tobacco smoke), behaviors (e.g., diet, history of asthma) or complications (e.g., early labor, maternal health complications) during pregnancy may contribute to the development of asthma and other respiratory illnesses in offspring.

Hypothesis #4: Exposures to environmental agents found in the home, such as environmental tobacco smoke (ETS) or indoor allergens, in early childhood may lead to the development or exacerbation of asthma.

Hypothesis #5: Exposure to air pollutants such as ozone and particulate matter may lead to the development or exacerbation of asthma.

Targeted Research Area: Childhood Cancers

Hypothesis #6: Exposure to electromagnetic fields (EMFs) may increase the risk of childhood cancers such as leukemia (acute lymphocytic and T-cell) and brain tumors.

Hypothesis #7: Exposure to solvents and paints may increase the risk of childhood cancers, including leukemia and brain tumors.

Hypothesis #8: Exposure to insecticides/pesticides may increase the risk of childhood cancers, including leukemia and lymphomas.

Hypothesis #9: Exposure to paternal/maternal smoking may increase the risk of childhood cancers, including brain tumors, and may increase the risk of lung cancer in adulthood.

Hypothesis #10: Exposure to infectious agents/viruses may increase the risk of childhood cancers, including brain tumors, and may increase the risk of lung cancer in adulthood.

Targeted Research Area: Endocrine Disrupters

Hypothesis #11: Increased fetal exposure to endocrine disrupters may result in reproductive and physiological abnormalities.

Targeted Research Area: Environmental Toxicants

Hypothesis #12: Exposure to contaminants in water, such as chlorine disinfection byproducts, can lead to adverse birth outcomes such as neural tube defects, low birth weight, and spontaneous abortions.

Hypothesis #13: Exposure to environmental toxicants, such as air pollutants and DEHP (di-2-ethylhexyl phthalate), can affect various stages of child development, from intrauterine to postnatal development.

Hypothesis #14: Exposure to environmental toxicants such as pesticides (e.g., organophosphates) can play a causal role in childhood diseases ranging from asthma to neurological disorders.

Targeted Research Area: Injury

Hypothesis #15: Factors in the immediate environment surrounding children (e.g., instability in the home, household composition), can be major risk factors in the incidence of childhood injury.

Hypothesis #16: Children who are exposed to physical and psychological stress due to large disruptions in their broader community/social environment, such as war, natural disasters (e.g., hurricanes, bombings, large-scale accidents such as crashes), and poverty may be at high risk for developing complex psychological problems (in addition to physical injuries) due to deaths in the family, home damage, and displacement.

Hypothesis #17: As children grow and spend more time in the exterior environment, they are exposed to factors in the modern built environment that place them at risk for injury and death. The quality and structural safety of buildings, traffic, and play areas may affect the chance of incurring illness, disability, or injury. Poor construction and structural hazards may be leading causes for the prevalence of childhood falls, burnings, drownings, and secondary harms and diseases.

Hypothesis #18: Children may be at high risk for injury due to psychosocial factors in environments outside the home. Children who experience psychosocial stress in schools may be prone to aggressive or violent behavior, resulting in unintentional and/or intentional injury to oneself and others. School environments that exhibit high rates of psychosocial problems may also exhibit high rates of sports-related injuries among children and physical violence between children.

Targeted Research Area: Neurodevelopment and Biobehavioral Development

Hypothesis #19: Organophosphate pesticides such as PCBs, PCDDs, and PCDFs have a detrimental impact on neurodevelopment, causing functional, neurologic, and cognitive expression.

Hypothesis #20: Autism is a neurodevelopmental disease that may be linked to components of vaccines and immunizations and may have a genetic link.

Hypothesis #21: Stress, neglect, and trauma caused by child abuse and maltreatment have adverse affects on a child's neurodevelopment.

Hypothesis #22: Maternal immune response to infections can have an adverse effect on the fetus' neurodevelopment.

Hypothesis #23: In utero and postnatal exposure to methylmercury has adverse effects on a child's neurodevelopment and biobehavioral development.

Hypothesis #24: In utero and postnatal exposure to lead has adverse effects on a child's neurodevelopment and biobehavioral development.

Hypothesis #25: Exposure to lead impairs fetal biobehavioral development by lowering IQ and increasing cognitive developmental dysfunction.

Hypothesis #26: Maternally related factors such as smoking, exposure to environmental tobacco smoke, and substance abuse during pregnancy negatively affect biobehavioral development.

Hypothesis #27: Broader societal factors such as neighborhood and community conditions can adversely impact a child's biobehavioral development.

Targeted Research Area: Other - Obesity

Hypothesis #28: Altered intrauterine environment can affect fetal development leading to childhood obesity. Contributing factors include exposure to maternal diabetes, maternal malnutrition, and increased birth weight, which can alter fetal glucose tolerance and gene expression.

Targeted Research Area: Other – Sudden Infant Death Syndrome (SIDS)

Hypothesis #29: Infectious bacterial agents such as *Helicobacter pylori*, *Staphylococcus aureus*, and *Escherichia coli* and their toxins may be causal factors for SIDS.